REMARKS

Introductory Comments

Reconsideration of the above-identified application in view of the above amendments and foregoing arguments is respectfully requested.

Claims 10-16, 25, 33, 35, and 38 are pending and under consideration. Claim 30 has been canceled in this amendment. Claims 25 and 38 have been allowed. Claims 10, 11, 15 and 33 have been amended as explained below. No new matter has been added.

Applicants thank the Examiner for withdrawing the objection to the claims and the objection to the specification. Applicants thank the Examiner also for withdrawing the rejection of claims 10-16, 25, 30, 33, 35 and 38 under 35 U.S.C. § 112, first paragraph and the rejection of claims 25, 30 and 38 under 35 U.S.C. § 112, second paragraph. Finally, Applicants thank the Examiner for allowing claims 25 and 38.

Priority

The Examiner denies the Applicants' priority claim from Application Serial Number 08/869,579 with respect to the pending claims. The Examiner contends the priority date for the pending claims is the date of the present application, based on a lack of written description of the full length sequences of SEQ ID NOS: 5 and 17. Applicants strenuously traverse the Examiner's denial of Applicants' claim for priority.

The Examiner maintains his position as stated in the previous Office Action. Applicants traverse the Examiner's deny of priority, based on the same reasons presented in the prior responses. Applicants' arguments are incorporated herein. Applicants reserve the right to present these arguments for appeal.

Rejection of Claims 10-16, 33 and 35 Under 35 U.S.C. § 112, First Paragraph

Claims 10-16, 33 and 35 are rejected under 35 U.S.C. § 112, first paragraph because the specification does not reasonably provide enablement for the scope of the claims regarding sequences that are complementary to SEQ ID NOS: 5 and 17. Applicants respectfully traverse this rejection.

Specifically, the Examiner contends that the claims as written encompass many sequences that are complementary to SEQ ID NOS: 5 and 17, and that the specification does not provide sufficient guidance as to the myriad of variant sequences. Applicants refute the idea that there is a myriad of sequences that are complementary to SEQ ID NOS: 5 and 17.

First, Applicants would like to point out that the claims refer to SEQ ID NO: 5 and complements thereof. Claim 30 has been canceled and claims 25 and 38 have been allowed. The complements of SEQ ID NO: 17 is no longer an issue with respect to the pending claims.

Second, "complements" are known in the art to be those sequences that are complementary to a polynucleotide sequence. "Complementary" is defined by Lodish *et al.*, Molecular Cell Biology, Fourth Edition (W.H. Freeman and Company, 2000) as "Referring to two nucleic acid sequences or strands that can form a perfect base-paired double helix with each other". Therefore, the claims are not drawn to a myriad of variant polynucleotides or polypeptides as the Examiner suggests.

However, in order to expedite prosecution, Applicants have amended claims 10, 11, 15 and 33 to recite that the complements are the complete complements of SEQ ID NO: 5. SEQ ID NO: 5 contains at 68 nucleotides. The complete complements of SEQ ID NO: 5 therefore contain at least 68 nucleotides, and the at least 68 consecutive nucleotides must be completely complementary to those of SEQ ID NO: 5. Therefore, Applicants respectfully request withdrawal of the rejection of claims 10-16, 33 and 35 under 35 U.S.C. § 112, first paragraph because the specification does not reasonably provide

enablement for the scope of the claims regarding sequences that are complementary to SEQ ID NO: 5.

Additionally, claims 10-16, 33 and 35 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the art that the inventors, at the time the application was filed, had possession of the claimed invention. Specifically, the Examiner states that the claims as written, are drawn to a genus which does not place any limitations on the number of amino acid substitutions, deletions, insertions and therefore variants.

Applicants submit that this argument is the same as presented above. Additionally, Applicants would like to point out the following.

The inquiry into whether the description requirement is met is determined on a case-by-case basis and is a question of fact. Section 2163 *Manual of Patent Examining Procedure* (8th Edition, Rev. 1, Feb. 2003). When a question regarding the adequacy of the written description arises, the fundamental factual inquiry is whether the specification conveys to those skilled in the art, as of the filing date sought, that applicant was in possession of the invention being claimed. Section 2163.02 *Manual of Patent Examining Procedure* (8th Edition, Rev. 1, Feb. 2003). Possession can be shown in a number of ways. For example, an Applicant can show possession by: (1) an actual reduction to practice of the claimed invention; (2) a clear depiction of the invention in detailed drawings or in structural chemical formulas which permit a person skilled in the art to clearly recognize that applicant had possession of the claimed invention; or (3) any description of sufficient, relevant, identifying characteristics so long as a person skilled in the art would recognize that the inventor had possession of the claimed invention. *Id.*

A description as filed is presumed to be adequate, unless or until sufficient evidence or reasoning to the contrary has been presented by the Examiner to rebut the presumption. Section 2163.04 *Manual of Patent Examining Procedure* (8th Edition, Rev. 1, Feb. 2003). The Examiner, therefore, must have a reasonable basis to challenge the adequacy of the written description. *Id.* The

Examiner has the initial burden of presenting by a preponderance of the evidence why a person skilled in the art would not recognize in an applicant's disclosure a description of the invention as defined by the claims. *Id.* "A general allegation of unpredictability in the art is not a sufficient reason to support a rejection for lack of adequate written description." *Id.* The *Manual of Patent Examining Procedure* even cautions Examiners that "rejection of an original claim for lack of written description should be rare." (See Section 2163 *Manual of Patent Examining Procedure* (8th Edition, Rev. 1, Feb. 2003)).

The U.S. PTO has issued Guidelines governing its internal practice for assessing whether the specification contains an adequate written description of the invention being claimed. In its Guidelines, the PTO has determined that the written description requirement can be met by "show[ing] that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics..., i.e., the complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics. Utility Examination Guidelines, Federal Register, Vol. 66, No. 4, pages 1092-1099, January, 2001 *Guidelines*, 66 Fed. Reg. at 1106.

Contrary to the arguments made by the Examiner, Applicants submit that the specification adequately describes the polynucleotides encompassed within the scope of the invention being claimed. First, as specifically recommended by the *Guidelines*, Applicants have provided the complete structure of the claimed polynucleotides as demonstrated in SEQ ID NOS: 5 and the complete complements thereof.

Second, with respect to the issue raised by the Examiner regarding the numerous structural variants, Applicants submit that because the level of skill in the area of molecular biology is considerably high, one of ordinary skill in the art, after reviewing Applicants' specification, would clearly recognize that the Applicants have provided an adequate written description of the variants, substitutions, deletions and/or additions encompassed by the claims. Applicants specifically direct the Examiner's attention to page 25, lines 4-16 of the

specification where it states that "Thus a polypeptide of the present invention may have an amino acid sequence that is identical to that of the naturally occurring polypeptide or that is different by minor variations due to one or more amino acid substitutions. The variation may be a "conservative change" typically in the range of about 1 to 5 amino acids, wherein the substituted amino acid has similar structural or chemical properties, e.g., replacement of leucine with isoleucine or threonine with serine. In contrast, variations may include nonconservative changes, e.g., replacement of a glycine with a tryptophan. Similar minor variations may also include amino acid deletions or insertions, or both. Guidance in determining which and how many amino acid residues may be substituted, inserted or deleted without changing biological or immunological activity may be found using computer programs well known in the art, for example, DNASTAR software (DNASTAR Inc., Madison, WI)." As illustrated by the above cited portion of the specification, computer programs are available to those of ordinary skill in the art and these programs can be used in providing guidance in determining "which and how" many amino acids residues in the polypeptides that are derived from polynucleotides SEQ ID NOS: 5 and the complete complements thereof, can be substituted, inserted or deleted. The use of such programs is well known to those of ordinary skill in the art. These programs and the determination of substitution, deletion or insertions are applicable to polynucleotides as well as polypeptides.

Additionally, page 11, line 22 to page 12, line 5 of the specification describes that methods for determining the percent identity are well known in the art.

Therefore, in view of the aforementioned arguments, Applicants submit that one of ordinary skill in the art would clearly recognize that Applicants had possession of the claimed invention and have provided an adequate written description. Thereupon, Applicants respectfully submit that the Examiner has failed to provide sufficient factual evidence to rebut the presumption that the description as filed is inadequate. Moreover, the Examiner fails to present any factual evidence as to why a person of ordinary skilled in the art would not

recognize in Applicants disclosure a description of the invention as defined by the claims. In view of the absence of such evidence, Applicants submit that this rejection should be withdrawn.

Finally, claim 30 is rejected under 35 U.S.C. § 112, first paragraph because the specification does not reasonably provide enablement for the scope of the claims for *in vivo* transfection in an animal. Applicants have canceled claim 30 and the rejection is now moot.

Rejection of Claims 10-16, 33 and 35 Under 35 U.S.C. § 102(b)

Claims 10-14, 33 and 35 are rejected under 35 U.S.C. § 102(b) as being anticipated by and also on sale and publicly used from Boehringer Mannheim Biochemical, 1991 catalog, page 557 (herein "Boehringer"), as cited in the previous Office Action. Specifically, the Examiner contends that Boehringer teaches and sells random hexamer primers that are complements to all nucleic acid sequences and which is available in a container. Thus, the Examiner alleges the hexamers read on the claims with respect to "complements". Applicants respectfully traverse the rejection.

Applicants' arguments above are incorporated herein. As indicated above, the claims have been amended to recite that the complements are the complete complements of SEQ ID NO: 5. Therefore, the claims cannot read on the six units hexamers of Boehringer becaue the claims now require a sequence that is at least 68 nucleotides in length. Applicants submit that the amendment has overcome the Boehringer art rejection and withdrawal of this rejection is respectfully requested.

Claims 11-16 and 33 are rejected under 35 U.S.C. § 102(b) as being anticipated by Stanchi *et al.*, WO 93/15197 (herein "Stanchi"). Applicants respectfully traverse the rejection.

The Examiner states that Stanchi discloses nucleic acids that are complements of SEQ ID NO: 5 and refers to the Sequence Comparison A, as provided by the Examiner. The Sequence Comparison A only shows 17 nucleotides matches to SEQ ID NO: 5. SEQ ID NO: 5 contains 68 nucleotides

and the claims have been amended to explicitly require the complements are the complete complements of SEQ ID NO: 5. Therefore, Stanchi does not disclose the claimed polynucleotides which are at least 68 nucleotides in length. Accordingly, Applicants respectfully request withdrawal of the rejection of claims 11-16 and 33 under 35 U.S.C. § 102(b) as being anticipated by Stanchi *et al.*, WO 93/15197.

Claims 10-14, 33 and 35 are rejected under 35 U.S.C. § 102(b) as being anticipated by Hillier *et al.*, EST Database Accession No. AA195677 alignment, 19 May 1997 (herein "Hillier"*)*.

The Examiner states that since the claims do not limit the length of the complements, the claims are anticipated by Hillier. Applicants respectfully traverse the rejection.

This issue has been addressed above. Applicants' arguments above are incorporated herein. As indicated above, the claims have been amended to recite the complements are the complete complements of SEQ ID NO: 5. Therefore, the claims cannot read on the polynucleotides of Hillier. Applicants submit that the amendment has overcome the Hillier art rejection and withdrawal of this rejection is respectfully requested.

Rejection of Claims 10-16, 33 and 35 Under 35 U.S.C. § 103(a)

Claims 10-16, 33 and 35 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Stanchi *et al.,* WO 93/15197 (herein "Stanchi") and further in view of Stratagene catalog, 1988, page 39 (herein "Stratagene"). Applicants respectfully traverse the rejection.

The Examiner applies Stanchi for its disclosure as indicated above. The Examiner applies Stratagene for its teaching of making a kit. The deficiencies of Stanchi was discussed above. Applicants' arguments are incorporated herein. Statagene does not cure the deficiencies of Stanchi. Therefore, Applicants respectfully request withdrawal of the rejection of claims 10-16, 33 and 35 under 35 U.S.C. § 103(a) as being unpatentable over Stanchi *et al.*, WO 93/15197 and further in view of Stratagene catalog, 1988, page 39.

Claims 10-16, 33 and 35 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Hillier *et al.*, EST Database Accession No. AA195677, alignment 19, May 1997 (herein "Hillier") in view of Expression of Cloned Genes in *E. coli.*, Sambrook *et al.*, Cold Spring Laboratory, 1989 (herein "Sambrook"). Applicants respectfully traverse the rejection.

The Examiner applies Hillier for its disclosure as indicated above. The Examiner applies Sambrook for its teaching of transfection. The deficiencies of Hillier are discussed above. Applicants' arguments are incorporated herein. Sambrook does not cure the deficiencies of Hillier. Therefore, Applicants respectfully request withdrawal of the rejection of claims 10-16, 33 and 35 under 35 U.S.C. § 103(a) as being unpatentable over Hillier *et al.*, EST Database Accession No. AA195677, alignment 19, May 1997 in view of Expression of Cloned Genes in *E. coli.*, Sambrook *et al.*, Cold Spring Laboratory, 1989.

CONCLUSION

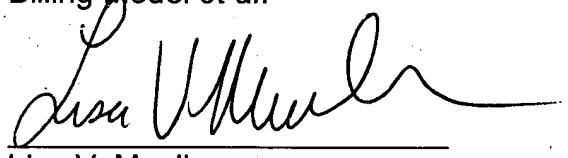
Applicants respectfully submit that the claims comply with the requirements of 35 U.S.C. Sections 112, 102 and 103. Accordingly, a Notice of Allowance is believed in order and is respectfully requested.

Should the Examiner have any questions concerning the above, she is respectfully requested to contact the undersigned at the telephone number listed below. If the Examiner notes any further matters which the Examiner believes may be expedited by a telephone interview, the Examiner is requested to contact the undersigned.

If any additional fees are incurred as a result of the filing of this paper, authorization is given to charge deposit account no. 23-0785.

Respectfully submitted,

Billing-Medel *et al.*



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